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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/446,200	05/19/95	FREEMAN G	RPI-033

EXAMINER

HM11/0331

LAHIVE & COCKFIELD, LLP
28 STATE STREET
BOSTON MA 02109

RABIN,E

ART UNIT	PAPER NUMBER
1644	12

DATE MAILED: 03/31/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 12/15/97

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire -3- month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-59 is/are pending in the application.
Of the above, claim(s) 5-59 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-4 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

–SEE OFFICE ACTION ON THE FOLLOWING PAGES–

DETAILED ACTION

Response to Amendment

1. Applicant's amendment was received December 15, 1997 as Paper No. 11.

2. Effective February 7, 1998, the location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1644, Technology Center 1600.

3. Claims 1-59 are pending. Applicant had traversed the restriction in Paper No. 7. Applicant's traversal of the restriction again is noted. For reasons set forth in Paper No. 8, the restriction is maintained. Applicant may petition the Commissioner to review the requirement.

This application contains claims 5-59, drawn to an invention non - elected with traverse in Paper No.7. A complete response to the final rejection must include cancellation of non - elected claims or other appropriate action (37 CFR 1.144) MPEP § 821.01.

4. Claims 1-4 are currently under examination.

5. Any rejection not present in this office action is considered withdrawn.

Claim Rejections - 35 USC § 103

6. Claims 1-4 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hathcock *et al.* [J. Exp. Med. 180: 631-640 (Aug 1994)] in view of Linsley *et al.* [U.S.

Patent 5,580,756 (102(e) Date: Mar 1990)], Kuchroo *et al.* [Cell 80: 707-718 (Mar 1995)] and Janeway *et al.* [Cell 76: 275-285 (Jan 1994)], for the same reasons as set forth in Paper No. 8.

7. Applicant's arguments filed December 15, 1998 have been fully considered, but they are not persuasive.

Applicant argues that the references fail to teach or suggest the claimed methods. Applicant further argues that the Examiner has not presented evidence that one having ordinary skill in the art would have been motivated to combine the teachings in the applied references to arrive at the claimed inventions.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation to induce a Th2-type response by contacting the population of activated CD4+ T cells with an agent which stimulates a B7-2 -induced signal is clearly set forth in the cited references. However, Applicant argues against the references in a piecemeal fashion.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In particular, Applicant argues that one of ordinary skill in the art would not have substituted soluble B72-Ig for the soluble B7 of Lindsley. However, the use of soluble receptors was well known in the art at the time of the invention. As evidence has come forth for interactions between membrane bound cell surface receptors and "partner receptors" in the interaction have been identified, the effects of soluble receptors, recombinant soluble receptors, and immobilized recombinant soluble receptors have been established. This pattern has been seen for more than a decade. Therefore, given the state of the art of the time of the invention and the motivation provided by the references, one would have substituted soluble B72-Ig for B72 in modulating an immune response.

Applicant further argues that Kuchroo *et al.* teach away from the claimed invention since stimulation with anti-B72 antibody results in increased IFNγ production, a characteristic of Th1-type cells. However, Kuchroo *et al.* clearly show on Page 715, Column 1 and Figure 7, as cited by the Examiner in Paper No. 8, "that the simplest interpretation of our data is that B7-1 preferentially acts as a costimulator for the generation of Th1 cells while B7-2 costimulates and induces Th2 cells (see model in Figure 7)." The claim recites "with an agent which stimulates a B7-2-induced signal". This would be interpreted by those in the art as an agent that acts in place of B7-2 to induce a signal on its partner, the counter-receptor of B7-2. The counter receptors of B7-2 are CD28 and CTLA-4. A stimulatory antibody interacting with the membrane bound B7-2 cell surface receptor would not be considered to be stimulating a B7-2-induced signal. In Figure 7, B7-2 is clearly depicted as interacting with CD28/CTLA-4, *i.e.,* as engaging in a B7-2-induced signal.

Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to stimulate CD3-activated T cells to differentiate to Th2 cells by activating them with immobilized soluble B7-2. One would have been motivated to

substitute soluble B7-2 for B7 in the teachings of Linsley *et al.* because of Hathcock's teaching of B7-2 on activated B cells, Kuchroo's teaching that interaction with B7-2 induces activated T cells to differentiate to become Th2 cells, and Linsley's teaching that immobilized soluble B7 is very effective. One would have been motivated to combine these teachings because signals involved in Th cell differentiation was a problem important in the art as evidenced by the teachings of Kuchroo *et al.* and Janeway *et al.*, for example. Based on the teachings of Linsley *et al.* and Kuchroo *et al.*, for example, one of ordinary skill in the art would have a reasonable expectation of success in modulating the immune response by immobilized, soluble, stimulatory B7-2. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Rabin, Ph.D. whose telephone number is (703)

305-6811. The examiner can normally be reached on Monday through Thursday from 7:30 AM to 6:00 PM.

10. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The FAX number for this Technology Center is (703) 305-3014 or (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center receptionist whose telephone number is (703) 308-0196.

Evelyn Rabin, Ph.D.
Patent Examiner
Technology Center 1600
March 30, 1998

Christopher Eisenschenk, Ph.D.
Primary Examiner
Technology Center 1600
March 30, 1998